

REMARKS

Claims 23 and 32-46 are pending. In the Office Action dated August 19, 2004, the Examiner rejected claims 23 and 32-46. Applicants have herein amended claims 23 and 32-43 and cancelled claims 44-46. Support for the amendments may be found throughout the specification, e.g., at page 3, lines 10-16; page 9, lines 30-35; and page 10, lines 1-10. No new matter has been added. Accordingly, claims 23 and 32-43 are pending.

In light of the amendments and the remarks herein, Applicants respectfully request withdrawal of the rejections and allowance of all claims.

Rejections under 35 U.S.C. § 102(b)

The Examiner rejected claims 23 and 32-46 under 35 U.S.C. § 102(b) over Sanders *et al.*, U.S. Pat. No. 5,766,605 (hereinafter “Sanders”) for the reasons of record in the prior office action. In particular, the Examiner asserted that the term “adixture” was unclear and that “there was no requirement in the claims for the composition to be mixed together.”

Applicants respectfully disagree with respect to the claims as currently amended. A claim is anticipated only if each and every element in the claim is found, either expressly or inherently, in a single prior art reference. *Verdegaal Bros. V. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). Claim 23 as amended recites a composition of matter that includes a solution of a botulinum toxin, a local anesthetic agent, and a local vasoconstrictive agent. At no point does Sanders teach or suggest the presently claimed compositions of matter. In Sanders, a sedative, a decongestant, a local anesthetic, and botulinum toxin were separately administered. Separate administration of a botulinum toxin, a local anesthetic, and a local vasoconstrictive agent does not anticipate a composition of matter that includes a solution of a botulinum toxin and either a local anesthetic agent or a local vasoconstrictive agent, or both. Moreover, separate administration of a botulinum toxin, a local anesthetic, and a local vasoconstrictive agent to a dog’s nares, as disclosed in Sanders, does not necessarily result in a composition of matter that includes a solution of a botulinum toxin, a local anesthetic, and a local vasoconstrictive agent, as required for anticipation by inherency. “The

mere fact that a certain thing *may result* from a given set of circumstances is insufficient to prove anticipation. . . . [The challenger] was required to prove that [a certain element] was necessarily present in the [prior art] disclosure, and that it would be so recognized by persons of ordinary skill . . ." Electro Medical Systems, S.A. v. Cooper Life Sciences, Inc., 34 F.3d 1048 (Fed. Cir. 1994) (emphasis in the original). Accordingly, Sanders does not expressly or inherently anticipate the presently claimed compositions.

Given all of the above, Applicants respectfully request withdrawal of the rejections under 35 U.S.C. § 102(b).

Rejections under 35 U.S.C. § 103

The Examiner rejected claims 23 and 32-46 under 35 U.S.C. §103(a) over Adams *et al.* (U.S. Patent No. 4,029,794) ("Adams") in view of Sanders for the reasons of record in the prior office action. In the prior office action, the Examiner asserted that Adams does not teach botulinum toxin and Sanders does not teach the vasoconstrictor epinephrine, but that it would be *prima facie* obvious to substitute botulinum toxin for saxitoxin and epinephrine for phenylephrine given the "reasonable expectation that the respective species will behave in a comparable manner or give comparable results in comparable circumstances as noted in Sanders."

Applicants respectfully disagree. Proper analysis under § 103 requires consideration of two factors: (1) whether the prior art would have suggested to those of ordinary skill in the art that they should make the claimed composition, and (2) whether the prior art would also have revealed that in so making, those of ordinary skill would have had a reasonable expectation of success. In re Vaeck, 947 F.2d 488, 20 U.S.P.Q.2d 1438 (Fed. Cir. 1991). Furthermore, with respect to chemical compositions, "[a] compound and all of its properties are inseparable; they are one and the same thing. . . . There is no basis in law for ignoring *any property* in making such a comparison." See In re Papesch, 315 F.2d 381 (C.C.P.A. 1963) (emphasis added).

Adams teaches a local anesthetic composition that includes a mixture of saxitoxin and a conventional local anesthetic compound. Contrary to the Examiner's assertion, however, it is not

obvious to "substitute the neurotoxin botulinum toxin for the neurotoxin saxitoxin," as Applicants respectfully assert that one having ordinary skill in the art would not consider the two compounds to be "equivalents." Saxitoxin and botulinum toxin have different chemical structures, different sites of action, and different mechanisms of action. For example, saxitoxin is a guanidinium alkaloid having the chemical structure: 3aS,4R,10aS)-2,6-diamino-4-[[[aminocarbonyl)oxy]methyl]- 3a,4,8,9-tetrahydro-1H,10H-pyrrolo[1,2-c]purine-10,10-diol. Botulinum toxin, on the other hand, is a large, alpha-helical protein having two subunits. Saxitoxin alters the action potential at voltage-gated sodium channels, while botulinum toxins block the release of acetylcholine at the neuromuscular endplate of neurons.

Saxitoxin and botulinum toxins also have different pharmacokinetic properties. As indicated in the specification, the paralysis induced by saxitoxin does not last as long as the paralysis induced by botulinum toxin, and repeated injections of saxitoxin would be needed. See page 7, lines 22-25. Furthermore, while saxitoxin may be used alone as a local anesthetic, the effective dose of saxitoxin is relatively close to the lethal dose in animals. Indeed, as noted in Adams at Cols. 7 and 8, saxitoxin was not effective at producing paralysis when administered alone at sub-lethal doses, while botulinum toxin alone has been extensively used for such purposes.

Given all of these differences in structure and mechanism of action, one having ordinary skill in the art would have no reasonable expectation that saxitoxin and botulinum toxin would act equivalently when combined in solution with a local anesthetic and/or vasoconstrictor. Applicants respectfully submit that there would thus be no reasonable expectation that the two neurotoxins would behave in a comparable manner or give comparable results in comparable circumstances. Accordingly, Applicants respectfully submit that the claims are not obvious given Adams in view of Sanders.

In light of all of the above, Applicants respectfully request the withdrawal of the rejections under 35 U.S.C. § 103.

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Page : 7 of 7

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CONCLUSION

Applicants respectfully assert that all claims are in condition for allowance, which action is requested. The Examiner is invited to telephone the undersigned if such would expedite prosecution.

Please apply any other charges or credits to deposit account 06-1050.

Respectfully submitted,

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